

10060765 0052102

Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PRODUCTS

Express Mail No. EV064987286US

Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

human FGF-21	MDSDETGFHSGLWVSVLAGLLLGACQAHPIPDSSPLLQFG-GQV-RQRYLYTD	52
	** * * * * * * ** * * * **	
mouse FGF-15	MARKWNGRAVARALVLATLWLAVS-GRPLAQ-QSQSVSDEDPLFLYGWGKITRLQYLYSA	58
	DAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYG	112
	* ** * * * * * * * * * ** **	
	GPYVSNCFLRIRSDGSDCEEDQNERNLLEFRAVALKTIAIKDVSSVRYLCMSADGKIYG	118
	SLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPAPFLPLPGLPP	172
	* * ***      *** * * * *      * *      * * *	
	LIRYSEEDCTFREEMDCLGYNQYRSMKHLHIIFIQAK-PREQLDQKPSNFIPVFHRSF	177
	ALPEPPGILAPQ--PPDVGSSDPLSMVGPSQG--RSPSYAS	
	*    * ** **      ***	
	FETGDQLRSKMFSLPLESDSMDPFRMVEDVDHLVKSPSFQK	

*Fig. 1*



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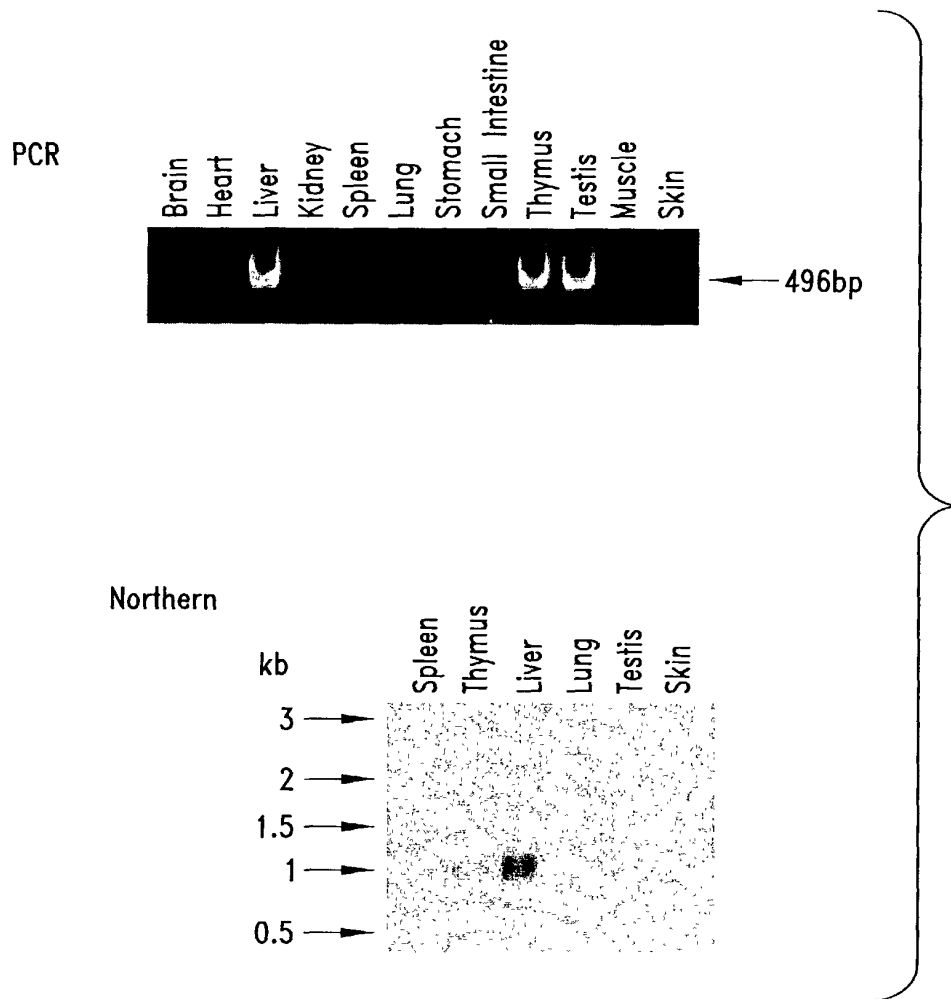
Human FGF-21	MDSDETFEHSGLWVSVLAGLLLG-ACQAHPIPDSSPLLQF--GGQVRQRYLYTDDAQ-	56
	* **** * * * * * * * *	
Human FGF-19	MRSGCVVHVW--ILAGLWLAVAGRPLAFSDAGPHVHYGWGDP IRLRHLYTSGPHGL	55
	TEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGS LHF	116
	* ** * * * * * * * * * * * * *	
	SSCFLRIRADGVVDCARGQSAHSLEIKAVLR T VAIKGVHSVRYLCMGADGKMQLLQY	115
	DPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPH--RDPAPRGP ARFLPLPGLPPAL	174
	* * * * * * * * * * * * * *	
	SEEDCAFE E EIRPDGYNVYRSEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEE	175
	PEP-PGILAPQ----PPDVGSSDPLSMV-GPSQGRSPSYAS	209
	** * * * * * * * *	
	PEDLRGHLESDMFSSPLETDSMDPFGLVTGLEAVRSPSF EK	216

*Fig. 2*

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*Fig. 3*

$$\begin{aligned} & \left( \frac{\partial}{\partial x^0} + v_1 \frac{\partial}{\partial x^1} + v_2 \frac{\partial}{\partial x^2} + v_3 \frac{\partial}{\partial x^3} \right) f(x) = 0 \\ & \text{where } v_i = \frac{\partial f}{\partial x^i} / \frac{\partial f}{\partial x^0}. \end{aligned}$$

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Filename: mouse FGF-21 cDNA in pGEM-T

Sequence Size: 659

Sequence Position: 1 - 659

Translation Position: 14 - 646

10	20	30	40	50	60	
GAGCGCAGCCCTGATGGAATGGATGAGATCTAGAGTTGGGACCCTGGGACTGTGGGTCCG						SEQ ID NO:1
M E W M R S R V G T L G L W V R						SEQ ID NO:2
70	80	90	100	110	120	
ACTGCTGCTGGCTGTCTTCCTGCTGGGGGTCTACCAAGCATACCCCATCCCTGACTCCAG						
L L L A V F L L G V Y Q A Y P I P D S S						
130	140	150	160	170	180	
CCCCCTCCTCCAGTTTGGGGGTCAAGTCCGGCAGAGGTACCTCTACACAGATGACGACCA						
P L L Q F G G Q V R Q R Y L Y T D D D Q						
190	200	210	220	230	240	
AGACACTGAAGCCCACCTGGAGATCAGGGAGGATGGAACAGTGGTAGGCGCAGCACACCG						
D T E A H L E I R E D G T V V G A A H R						
250	260	270	280	290	300	
CAGTCCAGAAAGTCTCCTGGAGCTCAAAGCCTTGAAGCCAGGGGTCAATCAAATCCTGGG						
S P E S L L E L K A L K P G V I Q I L G						
310	320	330	340	350	360	
TGTCAAAGCCTCTAGGTTTCTTTGCCAACAGCCAGATGGAGCTCTCTATGGATCGCCTCA						
V K A S R F L C Q Q P D G A L Y G S P H						
370	380	390	400	410	420	
CTTTGATCCTGAGGCCTGCAGCTTCAGAGAAGTGTGCTGCTGGAGGACGGTTACAATGTGTA						
F D P E A C S F R E L L L E D G Y N V Y						
430	440	450	460	470	480	
CCAGTCTGAAGCCCATGGCCTGCCCTGCGTCTGCCTCAGAAGGACTCCCCAAACCAGGA						
Q S E A H G L P L R L P Q K D S P N Q D						
490	500	510	520	530	540	
TGCAACATCCTGGGGACCTGTGCGCTTCCTGCCCATGCCAGGCCTGTCCACGAGCCCCA						
A T S W G P V R F L P M P G L L H E P Q						

*Fig. 4A*

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```
      550      560      570      580      590      600
AGACCAAGCAGGATTCCTGCCCCAGAGCCCCAGATGTGGGCTCCTCTGACCCCTGAG
D Q A G F L P P E P P D V G S S D P L S

      610      620      630      640      650      660
CATGGTAGAGCCTTTACAGGGCCGAAGCCCCAGCTATGCGTCCTGACTCTTCCTGAATC
M V E P L Q G R S P S Y A S *
```

*Fig. 4B*

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Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

Filename: human FGF-21 cDNA in pGEM-T

Sequence Size: 643

Sequence Position: 1 - 643

Translation Position: 9 - 638:

10	20	30	40	50	60	
agccattgatggactcggacgagaccgggttcgagcactcaggactgtgggtttctgtgc						SEQ ID NO:3
M D S D E T G F E H S G L W V S V L						SEQ ID NO:4
70	80	90	100	110	120	
tggtctgtcttctgctgggagcctgccaggcacaccccatccctgactccagtcctctcc						
A G L L L G A C Q A H P I P D S S P L L						
130	140	150	160	170	180	
tgcaattcgggggccaagtccggcagcgggtacctctacacagatgatgccagcagacag						
Q F G G Q V R Q R Y L Y T D D A Q Q T E						
190	200	210	220	230	240	
aagcccacctggagatcagggaggatgggacggtggggggcgctgctgaccagagcccg						
A H L E I R E D G T V G G A A D Q S P E						
250	260	270	280	290	300	
aaagtctcctgcagctgaaagccttgaagccgggagttattcaaatcttgggagtcgaaga						
S L L Q L K A L K P G V I Q I L G V K T						
310	320	330	340	350	360	
catccaggttcctgtgccagcggccagatggggccctgtatggatcgctccactttgacc						
S R F L C Q R P D G A L Y G S L H F D P						
370	380	390	400	410	420	
ctgaggcctgcagcttcgggagctgcttcttgaggacggataacaatgtttaccagtcgg						
E A C S F R E L L L E D G Y N V Y Q S E						
430	440	450	460	470	480	
aagccacggcctcccgctgcacctgccagggaacaagtccccacacgggaccctgcac						
A H G L P L H L P G N K S P H R D P A P						
490	500	510	520	530	540	
cccgaggaccagctcgcttctgccactaccaggcctgcccccgccactcccgagccac						
R G P A R F L P L P G L P P A L P E P P						

*Fig. 5A*

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      550      560      570      580      590      600
ccggaatcctggccccccagccccccgatgtgggctcctcggaccctctgagcatggtgg
  G I L A P Q P P D V G S S D P L S M V G

      610      620      630      640      650
gaccttcccagggccgaagccccagctacgcttcctgaagcca
  P S Q G R S P S Y A S *
```

*Fig. 5B*

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```
human FGF-21  MDSDETFEHSGLWVS-VLAGLLLGACQAHPIPDSSPLLQFGGQVRQRYLYTDDAQTEA  59
*             ****  **  ***  ** ***** * ***
mouse FGF-21  MEWMRSRVGTLGLWVRLLLAVFLLGVYQAYIPDSSPLLQFGGQVRQRYLYTDDDQDTEA  60

HLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPE  119
***** **  ***** ***** ***** ***** *****
HLEIREDGTVVGAHRSPESLLELKALKPGVIQILGVKASRFLCQQPDGALYGSPHFDPE  120

ACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPAPRFLPLPGLPPALPEPPG  179
***** **  **  *  ** ***** *
ACSFRELLLEDGYNVYQSEAHGLPLRLPQKDSPNQDATSWGPVRFLPMPGLLHEPQQDQAG  180

ILAPQPPDVGSSDPLSMVGPSQGRSPSYAS  209
* * ***** * *****
FLPPEPPDVGSSDPLSMVEPLQGRSPSYAS  210
```

*Fig. 6*



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Codon usage for yeast (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction	..
Gly	GGG	33.00	0.86	0.01	
Gly	GGA	70.00	1.82	0.02	
Gly	GGT	2672.00	69.62	0.91	
Gly	GGC	171.00	4.46	0.06	
Glu	GAG	277.00	7.22	0.10	
Glu	GAA	2442.00	63.63	0.90	
Asp	GAT	1100.00	28.66	0.48	
Asp	GAC	1211.00	31.55	0.52	
Val	GTG	117.00	3.05	0.04	
Val	GTA	75.00	1.95	0.03	
Val	GTT	1548.00	40.33	0.56	
Val	GTC	1026.00	26.73	0.37	
Ala	GCG	36.00	0.94	0.01	
Ala	GCA	203.00	5.29	0.06	
Ala	GCT	2221.00	57.87	0.65	
Ala	GCC	969.00	25.25	0.28	
Arg	AGG	20.00	0.52	0.01	
Arg	AGA	1336.00	34.81	0.83	
Ser	AGT	116.00	3.02	0.05	
Ser	AGC	94.00	2.45	0.04	
Lys	AAG	2365.00	61.62	0.78	
Lys	AAA	651.00	16.96	0.22	
Asn	AAT	347.00	9.04	0.22	
Asn	AAC	1259.00	32.80	0.78	
Met	ATG	766.00	19.96	1.00	
Ile	ATA	43.00	1.12	0.02	
Ile	ATT	1223.00	31.87	0.52	
Ile	ATC	1070.00	27.88	0.46	
Thr	ACG	28.00	0.73	0.01	

*Fig. 7A*

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Thr	ACA	126.00	3.28	0.06
Thr	ACT	1129.00	29.42	0.50
Thr	ACC	962.00	25.07	0.43
Trp	TGG	325.00	8.47	1.00
End	TGA	10.00	0.26	0.09
Cys	TGT	254.00	6.62	0.89
Cys	TGC	33.00	0.86	0.11
End	TAG	11.00	0.29	0.10
End	TAA	85.00	2.21	0.80
Tyr	TAT	219.00	5.71	0.19
Tyr	TAC	913.00	23.79	0.81
Leu	TTG	2202.00	57.38	0.69
Leu	TTA	576.00	15.01	0.18
Phe	TTT	432.00	11.26	0.27
Phe	TTC	1145.00	29.83	0.73
Ser	TCG	26.00	0.68	0.01
Ser	TCA	149.00	3.88	0.06
Ser	TCT	1279.00	33.33	0.52
Ser	TCC	818.00	21.31	0.33
Arg	CGG	0.00	0.00	0.00
Arg	CGA	1.00	0.03	0.00
Arg	CGT	249.00	6.49	0.15
Arg	CGC	5.00	0.13	0.00
Gln	CAG	62.00	1.62	0.05
Gln	CAA	1225.00	31.92	0.95
His	CAT	236.00	6.15	0.35
His	CAC	433.00	11.28	0.65
Leu	CTG	52.00	1.35	0.02
Leu	CTA	236.00	6.15	0.07
Leu	CTT	90.00	2.35	0.03
Leu	CTC	14.00	0.36	0.00
Pro	CCG	10.00	0.26	0.01
Pro	CCA	1271.00	33.12	0.80
Pro	CCT	279.00	7.27	0.18
Pro	CCC	33.00	0.86	0.02

*Fig. 7B*

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Codon usage for Drosophila (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction
Gly	GGG	6.00	0.28	0.00
Gly	GGA	380.00	18.04	0.22
Gly	GGT	575.00	27.29	0.34
Gly	GGC	746.00	35.41	0.44
Glu	GAG	1217.00	57.77	0.91
Glu	GAA	115.00	5.46	0.09
Asp	GAT	503.00	23.88	0.43
Asp	GAC	654.00	31.04	0.57
Val	GTG	719.00	34.13	0.45
Val	GTA	29.00	1.38	0.02
Val	GTT	226.00	10.73	0.14
Val	GTC	608.00	28.86	0.38
Ala	GCG	94.00	4.46	0.05
Ala	GCA	80.00	3.80	0.04
Ala	GCT	446.00	21.17	0.24
Ala	GCC	1277.00	60.61	0.67
Arg	AGG	48.00	2.28	0.06
Arg	AGA	12.00	0.57	0.01
Ser	AGT	16.00	0.76	0.01
Ser	AGC	267.00	12.67	0.23
Lys	AAG	1360.00	64.55	0.93
Lys	AAA	108.00	5.13	0.07
Asn	AAT	127.00	6.03	0.13
Asn	AAC	878.00	41.67	0.87
Met	ATG	387.00	18.37	1.00
Ile	ATA	4.00	0.19	0.00
Ile	ATT	390.00	18.51	0.29
Ile	ATC	969.00	45.99	0.71

*Fig. 8A*

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Thr	ACG	114.00	5.41	0.08
Thr	ACA	34.00	1.61	0.02
Thr	ACT	164.00	7.78	0.11
Thr	ACC	1127.00	53.49	0.78
Trp	TGG	243.00	11.53	1.00
End	TGA	1.00	0.05	0.01
Cys	TGT	20.00	0.95	0.08
Cys	TGC	220.00	10.44	0.92
End	TAG	12.00	0.57	0.17
End	TAA	58.00	2.75	0.82
Tyr	TAT	113.00	5.36	0.16
Tyr	TAC	574.00	27.25	0.84
Leu	TTG	210.00	9.97	0.12
Leu	TTA	9.00	0.43	0.01
Phe	TTT	62.00	2.94	0.09
Phe	TTC	635.00	30.14	0.91
Ser	TCG	195.00	9.26	0.17
Ser	TCA	29.00	1.38	0.02
Ser	TCT	103.00	4.89	0.09
Ser	TCC	558.00	26.49	0.48
Arg	CGG	7.00	0.33	0.01
Arg	CGA	25.00	1.19	0.03
Arg	CGT	281.00	13.34	0.34
Arg	CGC	465.00	22.07	0.55
Gln	CAG	703.00	33.37	0.91
Gln	CAA	66.00	3.13	0.09
His	CAT	88.00	4.18	0.22
His	CAC	312.00	14.81	0.78
Leu	CTG	1182.00	56.10	0.69
Leu	CTA	21.00	1.00	0.01
Leu	CTT	55.00	2.61	0.03
Leu	CTC	224.00	10.63	0.13
Pro	CCG	84.00	3.99	0.09
Pro	CCA	135.00	6.41	0.15
Pro	CCT	72.00	3.42	0.08
Pro	CCC	626.00	29.71	0.68

*Fig. 8B*

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Codon usage for enteric bacterial (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction . .
Gly	GGG	13.00	1.89	0.02
Gly	GGA	3.00	0.44	0.00
Gly	GGU	365.00	52.99	0.59
Gly	GGC	238.00	34.55	0.38
Glu	GAG	108.00	15.68	0.22
Glu	GAA	394.00	57.20	0.78
Asp	GAU	149.00	21.63	0.33
Asp	GAC	298.00	43.26	0.67
Val	GUG	93.00	13.50	0.16
Val	GUA	146.00	21.20	0.26
Val	GUU	289.00	41.96	0.51
Val	GUC	38.00	5.52	0.07
Ala	GCG	161.00	23.37	0.26
Ala	GCA	173.00	25.12	0.28
Ala	GCU	212.00	30.78	0.35
Ala	GCC	62.00	9.00	0.10
Arg	AGG	1.00	0.15	0.00
Arg	AGA	0.00	0.00	0.00
Ser	AGU	9.00	1.31	0.03
Ser	AGC	71.00	10.31	0.20
Lys	AAG	111.00	16.11	0.26
Lys	AAA	320.00	46.46	0.74
Asn	AAU	19.00	2.76	0.06
Asn	AAC	274.00	39.78	0.94
Met	AUG	170.00	24.68	1.00
Ile	AUA	1.00	0.15	0.00
Ile	AUU	70.00	10.16	0.17
Ile	AUC	345.00	50.09	0.83
Thr	ACG	25.00	3.63	0.07
Thr	ACA	14.00	2.03	0.04
Thr	ACU	130.00	18.87	0.35

*Fig. 9A*

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Amino Acid	Codon	Number	/1000	Fraction . .
Thr	ACC	206.00	29.91	0.55
Trp	UGG	55.00	7.98	1.00
End	UGA	0.00	0.00	0.00
Cys	UGU	22.00	3.19	0.49
Cys	UGC	23.00	3.34	0.51
End	UAG	0.00	0.00	0.00
End	UAA	0.00	0.00	0.00
Tyr	UAU	51.00	7.40	0.25
Tyr	UAC	157.00	22.79	0.75
Leu	UUG	18.00	2.61	0.03
Leu	UUA	12.00	1.74	0.02
Phe	UUU	51.00	7.40	0.24
Phe	UUC	166.00	24.10	0.76
Ser	UCG	14.00	2.03	0.04
Ser	UCA	7.00	1.02	0.02
Ser	UCU	120.00	17.42	0.34
Ser	UCC	131.00	19.02	0.37
Arg	CGG	1.00	0.15	0.00
Arg	CGA	2.00	0.29	0.01
Arg	CGU	290.00	42.10	0.74
Arg	CGC	96.00	13.94	0.25
Gln	CAG	233.00	33.83	0.86
Gln	CAA	37.00	5.37	0.14
His	CAU	18.00	2.61	0.17
His	CAC	85.00	12.34	0.83
Leu	CUG	480.00	69.69	0.83
Leu	CUA	2.00	0.29	0.00
Leu	CUU	25.00	3.63	0.04
Leu	CUC	38.00	5.52	0.07
Pro	CCG	190.00	27.58	0.77
Pro	CCA	36.00	5.23	0.15
Pro	CCU	19.00	2.76	0.08
Pro	CCC	1.00	0.15	0.00

*Fig. 9B*